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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,286	12/21/2001	Michael J. Robarge	9516-048-999	6358

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EXAMINER	
CHANG, CELIA C	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 01/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/032,286	Applicant(s) ROBARGE ET AL.	
	Examiner Celia Chang	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *04/25/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. This application is a CIP of SN 09/972,487. Claims 1-67 are pending.

2. Claims 49-55, 57-59, 63-67 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of disorders known to be treatable by thalidomide analogous (e.g. claims 56, 60-62), does not reasonably provide enablement for claims 49-55, 57-59, 63-67. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in *scope* with these claims.

Initially, it is pointed to that the *scope* of claims 49-52, 64-67 encompassed the "modulating" of the production of TNF-α, IL-1β, or T-cell, which is incredible and lacks enabling support because no description or document can be found of record that one compound can both enhance or inhibiting i.e. modulating, biological processes *at the same time.*

In addition, it was described in the specification (pages 2-5) that compounds of the instant claims depend on its biological activity in inhibiting TNF-α, IL-1β, or stimulating IL-10/T-cell functionality. Such biological mediators are known as cytokines. It is well recognized in the art that biological functionality of cytokines or cytokine manipulation are highly complexed and unpredictable (see Vecchiarelli CA 135). While the instant compounds which are analogs of thalidomide is expected to have similar activity in treating specific diseases known for thalidomide such as myeloma, leukemia etc. does not render support for the scope of the instant claims encompassing any and all implication of cytokine functionality. It is recognized in the art that function and toxicology of cytokines are complexed, and while further studies when become available may give more information on generals, only specific cytokines for their specific end effect such as treating inflammation, can be relied upon (see Foster CA 136).

It is recommended that the claims be particularly pointed to the specifics i.e. inhibiting cardiac pathophysiology by inhibiting elevated TNF-α (see p.3-4) etc.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6, 9, 10, 12, 14, 16, 18, 20, 22, 24, 25, 28, 30, 34, 36, 37, 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Muller et al. WO 98/54170 (cited on 1449 of parent case).

Muller et al. '170 disclosed applicants compound in small genus well delineated, thus, constitutes anticipation. See p.10, formula IIB in its definition. The clear explicit description of Muller formula IIB with the particular disclosure that such compounds are biologically active provided evidence that such compounds lacks novelty since they have been described in a limited class with biological property which is tantamount to naming each member (In re Petering 133 USPQ 275) and placed the instantly claimed compounds in possession of the public (In re LeGrice 133 USPQ 365, In re Brown 141 USPQ 245).

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-67 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mullet et al. US 5,635,517 in view of Muller et al. WO 98/54170, Bundgaard, Naik CA 118 and Smith et al. WO97/45117.

Determination of the scope and content of the prior art (MPEP §2141.01)

Muller et al. '517disclosed aminoisoindolylpiperidine similar to the claims (see col. 11, claim 4) composition and method for reducing undesirable TNF-α as the instant claims (see claim 1 and examples 3-5).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Muller et al. disclosed all the elements of the claim **except** the compound of Muller '517 is a "drug" instead of the instant prodrug i.e. N-acylated compounds. The preparation of the prodrug has been well recognized by artisan in the field (see Bundgaard textbook, Naik CA) and specifically taught by Muller '170 (see recited supra).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would find the instant claims prima facie **because** the preparation of a prodrug for a drug with free amino moiety is well recognized in the art (see Bundgaard and Nail) and enabled (see Muller '170). Especially, it is taught in the art that similar isoindolylpiperidines compounds i.e. thalidomide, are known for its extreme side effects which can be relieved by prodrug formulation (see Smith '117, col. 4 lines 1-5). One skilled in the art in possession of such acylated compounds and the skill of preparation in a varieties of prodrug formulation for free amines would be motivated to prepare the instant prodrugs with the expectation that such compounds would have similar activity when systemically administered and with less side effects.

5. Claims 1-67 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,395,754. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims fully embraced all the compounds, composition and method claims of 6,395,754.

Claims 1-67 are rejected under judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10 of Muller et al. US 5,635,517 and claims 1-12 of US Patent 6,395,754 in view of Bundgaard, Naik CA 118 and Smith et al. WO97/45117.

Determination of the scope and content of the prior art (MPEP §2141.01)

Muller et al. '517disclosed aminoisoindolylpiperidine similar to the claims (see col. 11, claim 4) composition and method for reducing undesirable TNF-α as the instant claims (see claim 1 and examples 3-5).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Muller et al. '517 disclosed all the elements of the claim **except** the compound of Muller '517 is a "drug" instead of the instant prodrug i.e. N-acylated compounds. The preparation of the prodrug has been well recognized by artisan in the field (see Bundgaard textbook, Naik CA) and specifically claimed by Muller '754, see claims 1-12.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would find the instant claims prima facie **because** the preparation of a prodrug for a drug with free amino moiety is well recognized in the art (see Bundgaard and Nail) and claimed by Muller '754, claims 1-12. Especially, it is taught in the art that similar isoindolylpiperidines compounds i.e. thalidomide, are known for its extreme side effects which can be relieved by prodrug formulation (see Smith '117, col. 4 lines 1-5). One skilled in the art in possession of such acylated compounds and the skill of preparation in a varieties of prodrug formulation for free amines would be motivated to prepare the instant prodrugs with the expectation that such compounds would have similar activity when systemically administered and with less side effects.

Claims 1-67 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-116 of copending Application No. 09/972,487. Please note that the complete scope of the copending application 09/972,487 is included in the instant claims 1-67.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

OACS/Chang
Jan. 22, 2003

Celia Chang
Primary Examiner
Art Unit 1625